

**AMENDMENTS TO THE SPECIFICATION:**

Please replace the paragraph beginning on page 1, line 21, with the following amended paragraph:

This is a continuation of U.S. Application Serial No. 07/552,719, filed July 16, 1990, which is a continuation of U.S. Application Serial No. 06/506,098, which is a continuation-in- part of commonly assigned U.S. ~~applications~~ Application Serial Number No. 06/488,323, filed April 25, 1983 and Serial Number \_\_\_\_\_, filed \_\_\_\_\_ (Attorney Docket 100/173).

This application is related to commonly assigned applications Serial No. 06/438,236 filed November 1, 1982, now U.S. Pat. No. 4,775,622, and its parent, and Serial No. 06/488,337, filed April 25, 1983, now abandoned, ~~which was filed as a continuation having Serial No. 07/541,186 filed June 20, 1990, now issued as U.S. Pat. No. 5,010,003,~~ the disclosures of which are hereby incorporated by reference.

Please delete the paragraphs beginning at page 8, line 33, which starts with "Fig. 13 depicts a Southern hybridization . . ." and ending with "Fig. 17 is a schematic of the construction of plasmid pR1."

Please replace the paragraph beginning on page 21, line 21, with the following amended paragraph:

The expression of the first 4 genes was achieved by the insertion of EcoRI fragments into p65 as described above. The genes were obtained by EcoR1 digestion of plasmids containing them as described in US 438,128 filed Nov. 1, 1982 (BoIFN) (abandoned); US 297,380, filed Aug. 28, 1981, (HSA) (abandoned); and US 312,489 filed Oct. 19, 1981 ( $\gamma$ IFN) (abandoned in favor of Continuation S.N. 746,813, now U.S. Pat. No. 4,762,791) and elsewhere, e.g., in Interferons edited by Merigan, et al., Academic Press, Inc. (1982), Proceedings of the Symposium on "Chemistry and Biology of Interferons: Relationship to

Therapeutics", held March 8-12, 1982, Squaw Valley, California; Lawn, et al. Nucleic Acids Research 9, 6103 (1981); Gray, et al., Nature 295, 503 (1982). ~~U.S. 438,128 relates to the isolation and identification of DNA sequences encoding animal interferons and to the construction of recombinant DNA expression vehicles containing such DNA sequences operably linked to expression effecting promoter sequences and to the expression vehicles so constructed.~~

Please delete the paragraph inserted at page 21, after line 31, which starts with "The following detailed description is illustrative of the invention for the preparation . . ." through and including the paragraph which starts with "The expression plasmid was assembled by ligating together 0.2 micrograms of vector . . .".

Please replace the paragraph beginning on page 21, line 33 and ending on page 22, 14, with the following amended paragraph:

Because of the placement of the restriction sites in the t-PA and rennin genes it was not practical to construct expression plasmids directly as above, but a modified approach was taken. The construction of the t-PA expression plasmid is illustrated in Fig. 10 using plasmid pt-PATrp12 (60) to obtain the t-PA gene by excision with XbaI and BglII, pB1 (described in Serial No. 438,236, supra) and YEp13 (43). The rennin expression plasmid was assembled in analogous manner using the rennin gene obtained by XbaI-BclI excision of pRI (described in US 452,227 filed Dec. 22, 1982, abandoned). These two plasmids contain the LEU2 gene for selection in yeast. Therefore an  $\alpha$  leu2 yeast strain was used for transformation with these plasmids. The prorennin expression plasmid pR1 was constructed by incubating EcoR1-Pst I cleaved  $\gamma$ -IMM plasmid with 5' and 3' segments in the presence of T4 ligase.  $\gamma$ -IMM is a pBR 322 derived plasmid described in U.S. Appln. Serial No. 312,489, filed Oct. 19, 1981 (abandoned in favor of Continuation of S.N. 746,813, now U.S. Pat. No.

4,762,791) and Gray, et al., supra. US 452,227 describes construction of the expression plasmid pR1:

a. Isolation of Messenger RNA for Prorennine

The fourth stomachs of freshly slaughtered calves of less than one week of age were removed and transported on ice from Conti Meat Packing Company, Inc., Henrietta, new York, and the mucosa promptly dissected away from the supporting tissue.

Please delete the paragraph inserted at page 22, after line 9, which starts with "Polysomes were isolated from 217 grams of mucosa by the method of . . ." through and including the paragraph after line 13, which starts with "Plasmids were isolated from the selected transformed clones . . .".

Please delete the paragraph inserted at page 32, after line 23, which starts with "63. Blin and Stafford . . ." through and including the paragraph which starts with "84. Crea et al.".

**IN THE DRAWINGS**

Please delete Figures 13, 14, 15A, 15B, 16 and 17.